Chapter 14

Time and Place of Action of Sex-determining Factors in Ontogeny

In multicellular organisms there is a division of labor among the various cell types that constitute an individual. Although endowed with identical genetic constitutions, different somatic cell types in different parts of the body perform different functions. This is because many of the genes are turned on only in certain somatic cell types. The gene loci for component polypeptides of hemoglobin function only in erythropoietic cells. Skin cells and cells of liver parenchyma, no doubt, maintain these genes in their nuclei, yet these genes remain dormant. Similarly, the gene locus for the hormone, insulin, is activated only in Langhans islet cells of the pancreas. The above examples are given in order to demonstrate that every gene with a specialized function has a particular somatic cell type in which to express itself.

For generating energy, the glycolytic cycle and allied pathways are essential to all cells. Accordingly, the enzymes associated with the above mentioned pathways are found in all the somatic cell types of the body. Yet, even in these enzymes, we see evidence of differential activation of gene loci. Lactate dehydrogenase is one such enzyme. In mammals and birds, there are three gene loci for three different component polypeptides of this enzyme. Each enzyme molecule is a tetramer made of four polypeptides. The gene locus for the third polypeptide C is activated only in the testis of male mammals and birds upon sexual maturity and spermiogenesis (Goldberg, 1962; Blanco and Zinkham, 1962; Blanco et al., 1964). Thus, the C4-type lactate dehydrogenase is seen only in the testis containing spermatozoa. In all other tissue of males as well as in all the tissues of the female, we see only five isozymes made of A and B polypeptides in
all possible combinations: A4, A3B1, A2B2, A1B3, B4 (Markert, 1963). These findings on lactate dehydrogenase not only serve to re-emphasize the fact that each gene has a place of its own to assert itself, but also illustrates another important fact, that each gene has a time of its own to express itself. This latter point is more vividly revealed by the five gene loci for five different component polypeptides of hemoglobin which is a tetramer. While the gene locus for \( \alpha \)-chain remains active throughout the life span of man, the other four gene loci are selectively activated and inactivated in sequence at different developmental stages. When hematopoiesis first begins in the early human embryo, the hemoglobin produced is an embryonic type made of two \( \alpha \)-chains and two \( \varepsilon \)-chains. Subsequently, the fetal hemoglobin which is \( \alpha_2\gamma_2 \) is produced. The adult hemoglobins, on the other hand, use \( \beta \)- and \( \delta \)-chains. The two types of hemoglobins are \( \alpha_2\beta_2 \) and \( \alpha_2\delta_2 \).

From the above examples, it becomes quite clear that until the time and place of assertion of the sex-determining factors have been delineated, the mere statement that the mammalian \( Y \)-chromosome is very strongly male-determining lacks substance.

The question of time and place is particularly relevant in view of the more recent finding on the \( Y \)-chromosome of \textit{Drosophila}. In Chapter 13 it was stated that while the mammalian \( Y \) is a very strong male determiner, the \textit{Drosophila} \( Y \) is a dummy of no consequence. Yet, it has been known that although the XO-constitution of \textit{Drosophila} gives rise to the male with spermatogenesis, his spermatozoa are incapable of fertilization. Now it appears that the \textit{Drosophila} \( Y \), which remains entirely heterochromatic in all other cell types, unwinds itself in nuclei of primary spermatocytes and becomes euchromatic, asserting its genetic influence. It is assumed that without this assertion by the \( Y \) in primary spermatocytes, spermatozoa produced are defective (Meyer, 1963). It then follows that the \textit{Drosophila} \( Y \) has been misunderstood as a dummy, simply because its time of assertion comes at the very end of gametogenesis. Conversely, it may be said that the mammalian \( Y \) emerges as a very strong male determiner only because its time of assertion is at the very beginning of gonadal development. It is apparent that the mammalian \( Y \) behaves as a dummy in most adult somatic cells as well as germ cells. At what time of development, through which cell type, does the mammalian \( Y \) assert its male-determining influence? This question shall be examined step by step.